Application No.: 10/004,487 Amendment dated February 28, 2005

Reply to Office Action mailed November 28, 2004

Amendments to the Specification

Please replace paragraph [0016] with the rewritten paragraph provided below.

-- [0016] The present invention is an apparatus, system and method for performing parallel, stepwise chemical synthesis in a multi-well plate format. The present invention will be described using one example, namely, a 384-well high-throughput DNA synthesizer. The present invention has a much wider application as will be appreciated by those of skill in the art of polymer synthesis in light of the present disclosure. Although the present invention is based on phosphoramidite chemistry, it is in no way restricted by the actual chemistry, viz., it is amenable to implementation using photo-, acid- or any other monomer, dimer dimmer, trimer or multimer addition chemistry based generally on solid supports. Furthermore, unlike existing synthesizers the present invention has the distinct advantage of enabling very large economy of scale. --

Please replace paragraph [0044] with the rewritten paragraph provided below.

-- [0044] A variety of commercially available filters (with a range of screen sizes from 75 to 250μm) and membranes (with a limited range of pore sizes, typically < 0.5μm) were tested and are described below. The methods used to test the above criteria are as follows. The flow rate Rate of a fixed volume was deposited on the membrane and the time required for all of it to flow through the membrane, both with and without vacuum applied, was recorded. The wicking of one drop of deblock (visibly orange because it was mixed with activated phosphoramidite) was deposited on the membrane and observed to determine if it diffused readily. Finally, chemical compatibility was tested by observing the membrane as it soaked in a bath of each of the synthesis reagents (deblock, activator, cap A, cap B, and oxidizer). The ideal material should have a slow flow rate (without vacuum applied), should not wick and will be chemically resistant to all synthesis reagents. --

Please replace paragraph [00170] with the rewritten paragraph provided below.

-- [00170] During these studies it was determined that an optimal synthesis protocol based on an analysis of the trityl removed during the deblock steps (as indicated by the orange color observed during this step) and an analysis of post-synthesis Matrix Assisted Laser Desorbtion Ionization Mass Spectroscopy (MALDI) and High Performance Liquid Chromatography (HPLC) data could be used to track performance. --

Please replace paragraph [00175] with the rewritten paragraph provided below.

-- [00175] DNA Analysis Technique. The oligonucleotides made may be tested using several techniques. One such technique is Matrix Assisted Laser <u>Desorption Desorbtion</u>
Time of Flight Mass Spectroscopy (MALDI-TOF MS). MALDI is a very quick, accurate analytical device that is based on ionizing, and then accelerating, a sample in a vacuum tube. The longer an ionized sample (or analyte) takes to "fly" a given distance, the more massive it must be. MALDI is quick (96 samples may be analyzed in two hours), however, it does not produce quantitative data because the relative peak heights in the resulting spectrum do not imply relative amounts of the analyte to which those peaks correspond. Thus, the mass of the various analytes and, from that, the identity of that analyte in a sample, may be determined but the absolute amount of each cannot. The theoretical mass of a single stranded DNA sample is given by the following equation:

Theoretical mass (amu) = (number of base A *312.2)

- + (number of base T *303.2)
- + (number of base C *288.2)
- + (number of base G *328.2)
- 61<u>.</u>